REMARKS/ARGUMENTS

Claims 1-4, 6, 8, 13, 15 and 17-34 have been canceled without prejudice for representation in a continuing application.

Claims 9, 11, 12, 14, 46 and 52 have also been revised to provide reference to a "mammalian" 5T4. Support for this revision is provided at least on page 26, lines 10-12 of the instant application. The revision is made in the interest of advancing prosecution and to better tailor the claims to currently contemplated commercial embodiments of the invention. No acquiescence to any rejection of record is intended or made.

Claims 11, 14, 46 and 52 have been revised with respect to the term "modified", which is defined in the instant application at least on page 5, lines 22-24, and page 26, lines 7-9. The revisions thus expressly recite that which was implicitly meant by the term. No narrowing of the claim was intended or believed to have occurred.

Claims 47-49 have been revised to correspond to revisions made in the claims from which they depend.

No new matter has been introduced, and entry of the above claims is respectfully requested.

Restriction Requirement

Applicants acknowledge the withdrawal of the previous restriction requirement mailed August 22, 2003, to which a response was timely filed on September 22, 2003. Unfortunately, Applicants timely response did not prevent a lapse of over 19 months before further action occurred in this application.

With the withdrawal of the previous restriction requirement, claims 46-51 were withdrawn from consideration as being "independent or distinct" from the invention of claims 9-12, 14 and 16. Applicants respectfully traverse.

As an initial matter, claims 48 and 49 are dependent from claim 9 and so are directed to subject matter wholly within the scope of claim 9. Additionally, the allegations of claims 46, 47, 50 and 51 as being directed to a patentably distinct invention do not apply to claims 48 and 49. Therefore, Applicants respectfully submit that they have been improperly denied consideration of claims 48 and 49 and the "finality" of the current Action should be withdrawn to allow examination of claims 48 and 49.

Moreover, and with respect to claim 46 (and claims 47, 50 and 51 which depend therefrom), Applicants respectfully note that the allegation of claim 46 as being broader than claim 9 is misplaced. Claim 9 was directed to "non-human" 5T4 antigens or all such antigens, whether naturally occurring or not, so long as they are not a naturally occurring human 5T4 antigen. Claim 46, on the other hand, was directed to all "modified" 5T4 antigens (and so would not include naturally occurring non-human 5T4 antigens) that contain a 5T4 epitope. Thus claim 46 was, and continues to be, directed to a subgenus of the subject matter of claim 9. The revisions to claims 9 and 46 have not altered this fact.

Further evidence of claims 46, 47, 50, and 51 as being directed to the same invention as claims 9 and 11 is seen in a comparison of claims 11 and 46. Both are directed to vaccine compositions comprising 1) a modified 5T4 antigen that contains at least one epitope of a mammalian 5T4 antigen and 2) a pharmaceutically acceptable carrier.

Finally, the particular sequences recited in claim 51 are those of a murine 5T4 antigen. This subject matter of claim 51 is related to the subject matter of claim 48, which is also directed to murine 5T4 antigen.

In light of the above, Applicants respectfully submit that the withdrawal of claims 46-51 is misplaced and the claims rejoined and examined with claims 9-12, 14, 16, and 52. In particular, the withdrawal of claims 48 and 49 is believed to be very unusual.

Rejections under 35 U.S.C. §112, first paragraph

There are two rejections under 35 U.S.C. §112, first paragraph in the instant Action mailed July 13, 2005. The first begins on page 4 of the Action and the second on page 7. Applicants address these in turn.

First rejection under35 U.S.C. §112, first paragraph

The rejection beginning on page 4 was originally presented in the previous Office Action mailed March 19, 2003 with respect to the phrase "peptide epitope of 5T4 antigen" such that the 5T4 antigen containing it induces a CTL response. This rejection alleges that claim 14 is inadequately supported by the written description to demonstrate that the inventors had possession of the claimed invention at the time the application was filed. Applicants understand this to be based on an allegation that the claims "fail to comply with the written description requirement." Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of an inadequate written description has been presented.

In the response filed June 19, 2003, the above phrase was revised to recite "an HLA CTL peptide epitope of 5T4 antigen" such that the modified 5T4 antigen containing it induces a CTL response. Applicants also pointed out how the specification provides actual examples of peptides from two mammalian 5T4 antigens that bind human HLA A, which is a MHC Class I antigen in Example 10. The response also provided information on how it was known in the art, as evidenced by the availability of predictive software and a publication from 1994, as to the identification of epitopes of a known protein for efficient CTL induction.

The instant Action asserts, however, that the response was unpersuasive because i) "[t]he disclosure asks others to fully enable the claimed invention"; ii) "Applicants' own disclosure must be adequately disclose the invention"; iii) "[t]here is nothing in the disclosure that shows any CTL response was observed"; iv) "Applicants cannot rely on others to enable their claimed invention"; v) "the disclosure does not set forth any CTL epitopes"; and vi) it is not routine "to induce CTL against a self antigen, after all the claimed antigen is a tumor antigen which is self antigen."

Applicants respectfully submit that the above arguments are insufficient to overcome the "strong presumption that an adequate written description of the claimed invention is present when the application is filed" as set out in the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement (Federal Register Vol. 66, No.4, 1099 January 5, 2001, see page 1105, left column and the case law cited therein).

The statement of the rejection, however, does not appear to acknowledge this presumption and asserts an inadequate written description based in part on allegations that the disclosure does not "enable" the claimed invention.[1] This is seen in items i), iv), and vi) above. This focus on enablement seems to be consistent with the Federal Circuit's decision in *In re Donohue*,[2] which states that.

> "possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention."

Therefore, this part of the rejection appears to be based upon the allegation that the application has not "enabled" the CTL inducing epitopes as recited in the claims. But given the apparent knowledge in the art for making and using such epitopes and the ability to conduct repetitive experiments with enormous numbers of peptides to determine their activity, where is the unpredictability necessary to support the allegation of a lack of enablement? Where is the undue amount of experimentation necessary to make and use such epitopes given the disclosed 5T4 antigen sequences and the specific exemplary peptides provided in the instant disclosure? Applicants respectfully submit that there is no issue of undue experimentation or undue level of unpredictability and so the invention is adequately enabled for the skilled artisan. This level of enablement thus provides possession in light of the instant statement of the rejection and *Donohue*.

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[1] Applicants address this point simply because of the number of times the term "enable" and variations thereof appear in the statement of the rejection.

Moreover, and with respect to item vi), Applicants respectfully point out that this apparent concern is addressed in Example 12c and Table 11 (pages 60-62 of the instant application). This demonstrates that it is not impossible or undue to conduct immunotherapy with an antigen like 5T4.

With respect to items ii) and iii) above, Applicants respectfully point out that claim 14 has been revised to recite that the HLA CTL peptide epitope is that of a *mammalian* 5T4 antigen. This is supported by the specific sequences presented in the instant application, which include that of the human (SEQ ID NO:1), canine (SEQ ID NO:3), and murine 5T4 (SEQ ID NO:2) antigens as well as HLA CTL peptides of those sequences. Applicants have thus adequately disclosed the invention such that a skilled artisan would recognize that there was contemplation and appreciation, and therefore possession, of the claimed invention.

Applicants respectfully point out that it is well settled in U.S. patent law that there is no requirement for an actual "reduction to practice" of a claimed invention. Instead, constructive reduction to practice is sufficient under U.S. law to support patentability. But the instant rejection's focus on the need to demonstrate a CTL response, as in item iii) above, indicates that demonstration of an actual reduction to practice of a CTL response is being required. Where is the basis for such a requirement, especially in light of the demonstrated knowledge in the field regarding CTL inducing epitopes and how to make and use them?

Last, Applicants again point out that contrary to item v) above, the specific peptide embodiments in Examples 10 and 11 form a body of representative species that supports the scope of claim 14 as presented. Given this disclosure and information content, there is simply no *prima facie* case of an inadequate written description. Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn.

Second rejection under35 U.S.C. §112, first paragraph

The rejection beginning on page 7 alleges that claims 9-11 are inadequately supported by the written description to demonstrate that the inventors had possession of the

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[2] 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

claimed invention at the time the application was filed. Applicants understand this to be based on an allegation that the claims "fail to comply with the written description requirement." Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of an inadequate written description has been presented.

The basis of the rejection appears to be the term "non-human" as present in claim 9 (and now claim 12 as revised above). Applicants respectfully point out that the claims have been revised to also refer to "mammalian" such that the basis for the instant rejection is believed to have been obviated.

Nevertheless, Applicants note that the statement of the rejection asserts that "a written description of the other claimed sequences of 5T4 antigens should be disclosed to overcome this rejection." The alleged support for the rejection is the decision in *University of California v. Lilly*, where a disclosure of a single rat cDNA encoding rat insulin was held to be insufficient to support claims like those directed to "vertebrate" and "human" cDNAs encoding insulin.

The statement of the rejection then goes on to analogize the instant application's disclosure of a canine 5T4 antigen (SEQ ID NO:3) to the above decision. Applicants respectfully point out, however, that distinct from the *University of California v. Lilly* case, where only the single rat cDNA was disclosed, is the fact that the instant application also discloses a murine 5T4 antigen (SEQ ID NO:2).

Moreover, Applicants respectfully traverse the focus on the number of 5T4 antigens disclosed because the claims are not directed to the antigens *per se*. To the contrary, the claims are more focused on the concept of *mammalian* 5T4 antigen epitopes that may be used to immunize a subject against 5T4 bearing tumors. Applicants respectfully submit that there is an adequate disclosure of various *mammalian* 5T4 proteins and peptides to induce immune responses (see for example pages 49-52, Examples 3-7, and Figures 3-7 of the instant application.

Given this proper focus, Applicants respectfully submit that no *prima facie* case of an inadequate written description is present and this rejection may be properly withdrawn.

Rejections based on cited documents

There are multiple rejections based on cited documents in the instant Action mailed July 13, 2005. The first begins on page 5 of the Action and the others on page 9. Applicants address these in turn.

First rejection under35 U.S.C. §102(b)

The rejection beginning on page 5 alleges that claims 9-12, 16 and 52 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Stern et al. (USP 5,869,053). Applicants have carefully reviewed the cited document and the statement of the rejection and respectfully request clarification because no *prima facie* case of anticipation appears to be present.

The rejection appears to be based upon the view that Stern et al. inherently disclose the invention encompassed by claims 9-12, 16 and 52. The statement of the rejection asserts that

> [t]he state of art indicates that the glycoprotein of Stern et al. is highly identical to the Non-human. The product claimed has the same structure as the now claimed product. Moreover the claims of Stern patent are not directed to a protein having a specific characteristics, they are not directed to a human or non-human. As a pioneering invention claim of ,053 is subject to broad interpretation.

Applicants remain confused because as shown above, the rejection appears to simultaneously allege that Stern et al. disclose a "highly identical" protein but yet "has the same structure as the now claimed product." Applicants respectfully submit that the rejection cannot be based on both positions. Either Stern et al. disclose the identical structure and use as encompassed by the instant claims to support an assertion of anticipation based on inherency, or Stern et al. do not disclose the identical structure and use as claimed and so no anticipation based on inherency is possible. Applicants respectfully point out that no degree of "highly identical" is

sufficient to satisfy the requirements for anticipation if the claims do not encompass that which is alleged to be "highly identical."

Applicants also point out that the claims are directed to "non-human, mammalian" 5T4 antigens while Stern et al. only disclose a human 5T4 antigen. Thus the claims are directed to structures and uses of a 5T4 antigen that are different from, and so not anticipated by, the human 5T4 antigen disclosed by Stern et al.

Furthermore, and with respect to claims 12, 14, 16, and 52, Applicants respectfully point out again that Stern et al. provide no teaching, suggestion or other indication of generating an anti-tumor immunotherapeutic response *to a tumor in a subject* by immunization with a mammalian 5T4. Stern et al. simply provides no disclosure of the relevance of 5T4 antigen to anti-tumor immunotherapy.

Moreover, and to the extent that the above quote reflects that the rejection is based on the ***claims*** of the Stern et al. patent as anticipating the instant claims, Applicants vigorously traverse because the Stern et al. claims define a genus that does not anticipate the instant claims. Applicants respectfully point out that the Stern et al. claims define the metes and bounds of patent rights while the specification disclosed the particular work (species) that was performed. The particular work was based on a human 5T4 without any teaching, suggestion, or other indication of a non-human 5T4. Stern et al. cannot anticipate claims directed to "non-human, mammalian" 5T4.

In light of the foregoing, Applicants respectfully submit that no *prima facie* case of anticipation has been presented, and this rejection may be properly withdrawn.

Second rejection under35 U.S.C. §102(b)

The rejection beginning on page 7 alleges that claims 9-12, 16 and 52 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Stern et al. (WO 89/07947). Applicants have carefully reviewed the cited document and the statement of the rejection and believe it is based on the same grounds as the Stern et al. U.S. patent addressed above.

As with the U.S. patent, this Stern et al. document only relates to human 5T4 antigen and so cannot anticipate claims relating to a "non-human, mammalian" 5T4 antigen.

Moreover, and as with the U.S. patent, there is no teaching, suggestion or other indication of generating an anti-tumor immunotherapeutic response *to a tumor in a subject* by immunization with a mammalian 5T4. This Stern et al. document also provides no disclosure of the relevance of 5T4 antigen to anti-tumor immunotherapy. Accordingly, this Stern et al. document cannot anticipate or render obvious claims 12, 14, 16, and 52.

Accordingly, Applicants respectfully asserted that no *prima facie* case of anticipation is present for the reasons provided above with respect to the U.S. patent.

Rejection based on Myers et al.

The last rejection beginning on page 5 alleges that claims 9-12, 14, 16 and 52 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by, or under 35 U.S.C. §103(a) as allegedly obvious over, Myers et al. (JBC 1994). Applicants have carefully reviewed the cited document and the statement of the rejection and respectfully request clarification because no *prima facie* case of anticipation appears to be present.

Applicants respectfully point out that Myers et al. only disclose a cDNA encoding a human 5T4 antigen. This is in contrast to claims 9-11, which relate to a "non-human, mammalian" 5T4 antigen. Despite the allegation in the statement of the rejection that "Myers et al. taught the product that is now being claimed by the Applicants (see Figure 3)", Applicants respectfully do not understand how this applies to the instant claims. Figure 3, part a, shows an alignment of portion of the human 5T4 antigen with the leucine rich regions (LRRs) of a number of other proteins, none of which is a 5T4 antigen. Figure 3, part b, shows the alignment of the N- and C-terminal residues from human 5T4 antigen with other proteins, none of which is a 5T4 antigen. What does any of this have to do with the non-human 5T4 related subject matter of the instant claims?

With respect to claims 12, 14, 16, and 52, Applicants respectfully point out that contrary to the assertions in the instant rejection against claims 14 and 52, Myers et al. provide

no teaching, suggestion or any indication of using any peptide in a method of eliciting an anti-tumor response *to a tumor in a subject* as encompassed by claims 12, 14, 16 and 52. There is also no teaching, suggestion, or other indication of immunizing a subject to provide such an anti-tumor response. Moreover, the sequences in Figure 3 are not those of any peptide that has been isolated or otherwise prepared. To the contrary, they are just portions of the sequence from non-5T4 proteins that have been aligned for comparison purposes. There is simply no teaching, suggestion or other indication of using any of the proteins in Figure 3 in a method as claimed. Accordingly, Myers et al. cannot anticipate these claims.

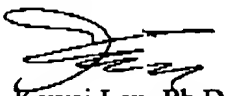
Furthermore, Myers et al. disclose no use of any peptide in immunization and no motivation to modify any peptide for use in the methods of claims 14 and 52. The knowledge in the art for the modification of peptides is irrelevant in the absence of any motivation to modify a particular peptide *for use in a method as claimed*. Applicants respectfully submit that no such motivation has been presented, and so no *prima facie* case of obviousness has been presented.

In light of the foregoing, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,



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